ANNUAL REPORT

OF

THE HOWE LABORATORY OF OPHTHALMOLOGY

HARVARD MEDICAL SCHOOL

AT THE

MASSACHUSETTS EYE AND EAR INFIRMARY

1964

243 CHARLES STREET

BOSTON, MASSACHUSETTS

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Laboratories, like people, reflect the care and problems which go into making them what they are. The Howe Laboratory has had sound parentage in the Harvard Medical School and the Massachusetts Eye and Ear Infirmary and a favorable environment in which to grow amidst an energetic and sympathetic community. That it has grown vigorously is not surprising; nor should it be surprising that crises arise recurrently when it "outgrows its breeches." Were it otherwise we should have cause to worry.

The year past has been one of adjusting burdgeoning research into inexpansible space. While the present Report gives a running account of some specific projects that have been, or are being, accomplished, an undetermined number of projects had to be jettisoned for lack of space. Within the next year we hope to resolve plans for a realistic expansion of our research facilities.

RESEARCH ACTIVITIES

Glaucoma

Research completed this year has included: 1) clinical evaluation of methyldopa in treatment of glaucoma; 2) study of after-effects of use of a-chymotrypsin in cataract extraction; 3) examination of the connections between blood vessels and aqueous outflow channels within the sclera of human eyes; and 4) investigation of the effects of use of alcoholic beverages in the presence of glaucoma.

These studies were all concerned with the very practical and important matter of learning what influences the intraocular pressure in glaucomatous patients, so that we may better know what may be used to the patient's advantage, as well as what should be avoided. The principal conclusions from these particular studies have been: 1) that methyldopa provides no improvement in control of glaucoma in human beings; 2) alpha chymotrypsin used as an aid in cataract extraction shows no tendency to cause permanent change in aqueous outflow in either glaucomatous or non-glaucomatous eyes; 3) contrary to classical concepts, aqueous outflow channels have relatively slight connection with blood vessels before they reach the outer surface of the human eye; therefore, the con-

dition of blood vessels within the sclera probably has little direct regulatory influence on aqueous outflow; 4) alcoholic beverages can be used in the presence of glaucoma without danger of raising the intraocular pressure; in fact they frequently lower the pressure significantly for several hours.

Certain glaucoma research projects already carried on for a number of years by Dr. Grant are long term systematic works still in progress. Such projects include: 1) clinical and experimental studies of glaucoma in infants and children; 2) functional measurements on the aqueous outflow channels of normal and glaucomatous human eyes; 3) comparison of calibration data for Schiotz and Applanation tonometers in sitting and recumbent positions; and 4) special punch-card compilation and correlation of the vast amount of information constantly accumulating on glaucomatous patients.

The experimental and clinical research in glaucoma under Dr. Grant's supervision is closely associated in the Howe Laboratory and in the Massachusetts Eye and Ear Infirmary's Glaucoma Consultation Service. Funds for research on glaucoma supervised by Dr. Grant are used to support work simultaneously in the Howe Laboratory and in the Glaucoma Consultation Service, according to the nature of the particular problems under investigation, and the space available. The ophthalmic residents each spend three months in the Glaucoma Consultation Service, where they are encouraged to develop an inquiring attitude and to join in the clinical research which is carried on principally by research fellows. The Fellowships in Glaucoma have been held this year by Dr. Jose E. Peczon and Dr. Vicente L. Jocson.

Histopathology

Although we have a department of experimental pathology separate from the department of clinical pathology, the two work in close affiliation and much of the research here described has resulted from the joint enterprise of the two departments. The former is headed by Dr. Kuwabara and the latter by Dr. Taylor Smith.

The interrelationship of neurones and glia in the retina has been a major preoccupation of some of us over the past several years. As noted in previous Reports one of the chief functions of glia is to

provide, in association with blood vessels, a homeostatic mechanism for the storage and retrieval of metabolic substrates for the retinal neurones. Dr. Kuwabara has now extended these studies to the pathologic retina. Retinas were damaged either mechanically, by producing a tear in the retina and subsequently injecting blood into the vitreous, or chemically, by injecting iodoacetate intravenously or acetic acid intravitreally. The consequent retinal changes in experimental animals were studied histochemically and electron microscopically for varying time periods, and then compared with the changes in pathologic human eyes obtained from the operating room. The main conclusion, reported this past year by Dr. Kuwabara at the International Congress of Histochemistry, was that Müller's cells are the first to show pathologic changes after injury to the retina. These changes consist of increased insinuation of Müller processes throughout the retina, migration of Müller cell nuclei toward the outer layer of the retina, and increased activity of several enzymatic reactions in Müller cells. The type of injury to the retina does not seem to be important. These retinal changes thus differ from those of the brain where proliferation of astrocytes and inflammation is the characteristic reaction to injury.

Poisoning of the retina by systemic iodoacetate administration has long been an experimental model for causing selective degeneration of the rod and cone cells. Dr. Kuwabara now finds by electron microscopy that the initial morphologic changes are in the synaptic organs between the rod and cone cells and the bipolar cells. These synaptic organs develop large vacuoles, their mitochondria show an increased electron density, and eventually the entire synapse disintegrates. Only a day or so after these changes commence in the synapses do the changes in the rods and cones appear.

The availability of a radioactive technique for labelling nascent cells by means of tritiated thymidine has given Drs. Richard Robb and Kuwabara an opportunity to explore the origin of cells involved in wound healing of the cornea. Autoradiographs have indicated to these investigators a marked proliferation of the stromal cells adjacent to a wound with little or no participation by the epithelium in stromal healing. With wounds of the central cornea no significant migration of cells occurred from the limbus.

The histologic studies on corneal wound healing were supplemented by electron microscopy. Dr. Kuwabara and Miss Barbara Bridgman confirmed at the ultramicroscopic level the observation that sliding of corneal epithelium involves primarily the superficial epithelial cells. The desmosomes do not lyse collectively but rather let go at the far end of a cell, away from the wound, while forming new attachments at the advancing end in a hand-over-hand manner. These changes become evident as early as one hour after wounding. Once these superficial cells cover the abraded area they gradually revert to a basal cell type and form new basement membrane.

Through the cooperation of the Children's Medical Clinic of Boston, Drs. Cogan and Kuwabara were able to study clinically and pathologically a series of eyes in patients with the so-called 13–15 trisomy. This recently recognized entity results from an anomalous extra chromosome in the 13–15 group. Ocular abnormalities are frequently part of the syndrome. The present study, which is the first to have been made on a sizeable series (12 cases), established the presence of intraocular cartilage as a common, and possibly pathognomonic, feature of the ocular abnormality. The pathogenesis of the cartilage is obscure.

Senile atrophy of the retina is frequently assumed to be caused by obliteration of the choriocapillaris. This in turn is attributed to progressive sclerosis and occlusion of the feeding arterioles. Drs. Friedman and Taylor Smith, however, have not confirmed this opinion in their study of flat mounts of the senile choroid. Obliteration of the choriocapillaris has been found related topographically to the imprint of large choroidal vessels on the capillary layer rather than to sclerotic occlusion of the arterioles.

Pursuing his interest in β glucuronidase, Dr. Hayashi has explored the distribution of this enzyme in the eye and in other tissues by means of a specific histochemical test which he devised. He has shown a good correlation between this histochemical method of demonstration and an homogenate assay. In the eye appreciable amounts of β glucuronidase have been found only in the pigment epithelium. Elsewhere it has been found significantly in macro-

phages, reticular cells, lymph nodes, Küpffer cells, pericytes of brain capillaries, and leucocytes.

Reviewing twenty-seven limbal epitheliomas, Drs. John Carroll and Kuwabara have offered a classification based on cell types. These tumors were found divisible into those containing characteristically either basal cells, prickle cells, clear cells, or goblet cells. Of these the basal cell type was the most frequent (52%) followed by prickle cell (33%), clear cell (11%) and goblet cell (4%). None of the cases metastasized but one-third (predominantly the basal cell type) have recurred. This classification should bring some order to this heterogeneous group of tumors which have heretofore been collectively called Bowen's tumor or carcinoma-in-situ.

An unusual case of leukemic tumors of the retina has been described by Drs. Kuwabara and Lloyd Aiello. Infiltration of the retina is relatively common with leukemia but the present case is believed to be the first to have shown proliferating tumors within the retina.

Our two electron microscopes continue to provide great service, not only for experimental studies but for observations on various pathologic conditions. In the previous Report we noted the observations of Drs. Kroll and Kuwabara on rhabdomyosarcoma of the orbit, melanoma of the choroid, and abiotrophy of the retina. This past year similar studies have been initiated on fine tissue changes in dysthyroid myopathy, in cystinosis, and in the curious entity of ataxia telangiectasia. The use of the electron microscope in the study of disease is still in the exciting stage of newness.

Biochemistry of the Lens

Although cataract formation has long been associated with swelling of the lens, the first clear exposition of this relationship was Dr. Kinoshita's concept of osmotic imbalance in sugar cataracts. The presence of polyol dehydrogenase and the availability of ample TPNH makes for the accumulation of the sugar alcohols which cannot be discharged from the lens fibers. Cataracts then result from the overhydration and eventual bursting of these fibers. This concept has been further consolidated this past year by Dr. Kin-

oshita, Dr. Hayman, and Mr. Merola, again using galactose cataracts in rats as the chief experimental model.

The maturation of these cataracts occurs in two stages characterized first by vacuolization of the cortex and secondly by opacification of the nucleus. During the vacuolar stage electrolytes do not increase in the lens indicating that movement of salt into the lens does not accompany the movement of water. In the interval between the vacuolization of the cortex and opacification of the nucleus no major change in lens hydration occurs and the content of dulcitol (galactose alcohol) remains as high as in the initial vacuolar stage. But the efficiency of the cationic pump decreases during this interval so that sodium can no longer be effectively excluded from the lens and the store of potassium steadily declines.

The stage of nuclear opacification or mature cataract develops with remarkable rapidity, usually within the period of a few hours. The accompanying chemical changes are similarly drastic. Both water and salt now increase markedly and the lens undergoes an acute further swelling. At first it was assumed that this late stage of maturation occurred when the cation pump finally failed, but other evidence indicates that the cation transport mechanism is as active in the mature as in the immature stage of cataractogenesis. It therefore seems likely that the major electrolyte changes result from some rapid alteration in the permeability barrier of the lens or lens fibers. An increase in membrane permeability could result in an influx of sodium more rapidly than could be counteracted by the pump mechanism. When this increased sodium influx can no longer be balanced by potassium efflux, chloride moves into the lens with the sodium to maintain osmotic equilibrium. At the same time, the dulcitol concentration drops owing, presumably, to the increased permeability. We thus have, for the first time, a biochemical basis for the understanding of one type of cataract.

Attention has been called in the recent literature to the early loss of amino acids from the lenses of galactose-fed rats and it has been suggested that the galactose poisons the lens. If the sugar alcohol—osmotic concept of cataractogenesis is correct, the loss of amino acids should be related to either the accumulation of dulcitol or the swelling of the lens. To test these possibilities a lens culture technique was employed in which it was first shown that the lens could concentrate amino acids against a gradient. High

levels of galactose in the medium impaired this amino acid uptake in proportion to the swelling of the lens. If, on the other hand, the lens is prevented from swelling by appropriate osmotic adjustment of the incubation medium, the uptake of amino acids is maintained at nearly normal levels. Thus, contrary to prevailing opinion, the loss in capacity for concentrating amino acids is due to hydration of the lens with its attendant changes in permeability rather than to a toxic or competitive action by galactose.

Preliminary observations have been made by Dr. Kinoshita on the effect of collagenase and other proteolytic enzymes on the lens. Collagenase can digest the lens capsule without affecting the epithelium or lens substance. Lenses thus decapsulated were found to possess normal rates of transport for amino acids and cations and to be able to maintain the normally high levels of glutathione and ascorbic acid. Apparently the capsule does not contribute to the permeability properties of the lens but serves simply for mechanical support.

The manner in which lens proteins are synthesized provides another approach to the study of lens metabolism. It is well known that lens proteins are being continually manufactured and degraded but Dr. Spector has found that one particular fraction comprising less than 10% of the total protein is synthesized more than three times as rapidly as any other soluble lens protein. The possibility is being explored that this may be a key intermediate in the synthesis of lens protein.

Another noteworthy observation of Dr. Spector's is that portions of the lens which do not contain DNA continue nevertheless to manufacture proteins. Apparently the RNA, template material for protein synthesis, is stable for long periods after disappearance of the DNA. We know of no other tissues which thus continues to synthesize protein through the stable RNA after disappearance of its master codifier.

In his study of hypoparathyroid cataracts, Dr. Thoft has succeeded in getting some positive results after cauterization of the parathyroid glands in rats. Yet this animal provides a poor experimental model since the cataracts do not appear until four to six weeks after the procedure and then regress gradually. Moreover the yield is low and the amount of tissue available is therefore insufficient for comprehensive biochemical study. Accordingly Dr.

Thoft has switched to the in vitro cultures of lenses incubated in media low in calcium thus mimicking a major aspect of hypoparathyroidism. This in turn has led to a determination of the role of calcium in lens metabolism.

The divalent calcium ion is found to influence profoundly the ability of the lens to accumulate ions and amino acids. Normally lenses accumulate potassium and alpha aminoisobutyric acid (AIB) efficiently so that the final concentration achieved in the lens is many times higher than that in the surrounding medium. In the absence of sufficient calcium, the lens fails to accumulate potassium or AIB and fails to extrude sodium effectively, suggesting an increased leakiness of the lens membranes.

To obtain quantitative data on the ionic exchange in and out of the lens, Dr. Thoft has devised a measure of the potassium flux based upon mathematical analysis of a two compartment system. Normal controls have shown approximately equal potassium fluxes for such widely different lenses as those of rats, rabbits, and calves. The determinations will now be applied to lenses in calcium-deficient media and the thesis explored that increased leakiness of the lens requires an increased activity of the cationic pump to maintain normal ionic balance. Cataracts are presumed to result from inability of the pump to keep up with the increasing leakiness of the membrane deprived of calcium.

Biochemistry of the Retina

Studies initiated in this Laboratory several years ago on the biochemical reactions associated with vitamin A metabolism, and recently on vitamin A esterification, have been directed this past year toward analysis of human retinal tissue. Dr. Futterman and Dr. Andrews have found that human retinal tissue can esterify vitamin A through reactions associated with operation of the visual cycle. The ester, isolated in pure form by procedures developed for this purpose and analyzed quantitatively, was found to contain a spectrum of saturated and monoenoic C_{12} to C_{18} fatty acids. As had previously been established for animals the major components, comprising 90% of the mixture, were found to be vitamin A palmitate, palmitoleate, stearate, and oleate. The fatty acid composition of vitamin A ester in human retinas thus differs markedly from that

of the retinal lipids in general which include principally palmitic, stearic, oleic, arachidonic, and docosahexaenoic acids.

With exposure of the retinal tissue to light the vitamin A formed from retinene in the outer segments of the visual cell migrates into the microsomes where the esterification reaction occurs. No additional supplements or cofactors are necessary in order to esterify the vitamin A in the microsomes. The microsomes manufacture a product whose fatty acid composition is identical to that of the vitamin A ester synthesized by the intact retina.

Because the source of vitamin A in the retina is the store of this vitamin in the liver, Drs. Futterman and Andrews have compared the vitamin A esters of the livers and retinas of a large number of vertebrates. They have found not only similar fatty acids in the two tissues but also esterification occurring in the microsomes in both cases. Esterification of cholesterol with fatty acids also takes place in the microsomes but at a different pH optimum and only in the presence of CoA and ATP.

Neuro-ophthalmology and Neurophysiology

Of the numerous patients with neuro-ophthalmic abnormalities which are referred to us, a few present conditions of sufficient rarity or are sufficiently informative to warrant detailed study. One entity which Drs. Goldstein and Cogan studied this past year was an apraxia of lid opening as manifested in four patients. This is characterized by impairment of volitional opening of the lids and in our patients was part of an extrapyramidal syndrome. It has not previously been distinguished from the common type of blepharospasm with compulsory closure of the lids. Another subject studied by Drs. Goldstein and Cogan was the effect of physical exercise on the visual symptoms of certain patients with the optic neuropathy of multiple sclerosis. In four patients physical exercise caused a transient worsening of the visual defect. No associated abnormality was found in the appearance of the retinal vessels, in the pressure of the retinal arteries, in the magnitude of the nystagmus (when present), or in the refractive status. Nor did artificially induced anoxia cause a change in the vision. On the other hand, three of the patients did observe a decrease in vision, similar to that induced by exercise, after taking a hot bath or after a heavy meal.

Hyperthermia is well known to cause a worsening of other manifestations of multiple sclerosis in some patients.

The visual and ocular motor signs in patients with bilateral cerebral lesions affecting the parietal, temporal, or frontal areas were analyzed in a group of 12 patients by Dr. Cogan. In addition to exaggeration of the visual agnosias and spatial disorientation which are sometimes symptomatic of unilateral lesions, some of these patients showed unique signs categorized under the headings of ocular motor apraxia and prolonged paralysis of conjugate gaze. These abnormalities were the substance of the Montgomery Lecture presented at the annual meeting of the Irish Ophthalmological Society.

Of continuing neurophysiologic interest has been Dr. Kupfer's study of changes in the lateral geniculate nucleus following sensory denervation, i.e. interruption of the optic nerve fibers. The observations reported last year of a decrease in several enzymes occurring concomitantly with a decrease in lateral geniculate cell size have been extended. In addition, histological and cytochemical changes in the lateral geniculate nucleus following visual deprivation (closing one eye) have been compared with those of sensory denervation in very young animals. Although a decrease in cell size occurred in both experimental situations, a decrease in enzyme activity occurred only following sensory denervation. This indicated that the lateral geniculate cells, although smaller following visual deprivation, were nevertheless carrying on potentially normal metabolic activities. These observations are relevant to the problem of amblyopia in children which occurs secondary to visual deprivation. These studies are being extended along quantitative biochemical lines.

In a recent two-month visit to University College, London, work was begun by Dr. Kupfer in collaboration with Dr. John Downer on the relationship of nucleic acid levels, protein synthesis and metabolic activity in lateral geniculate cells of the monkey following sensory denervation.

Also of neuro-ophthalmic note has been Dr. Fricker's development of objective methods for recording occipital signals from photic stimulation of the retina. For lack of space at the Infirmary Dr. Fricker was forced to develop the initial bulky equipment

elsewhere (actually in his garage). But he has now set up a miniaturized model at the Infirmary and is obtaining promising records on preliminary trials. By the combined use of sensors and computers he is obtaining quantitative measures of conduction-time in the eye-brain pathways and may be able to differentiate the sites of neuro-ophthalmic lesions by objective means. Its clinical importance remains to be seen.

Finally, Dr. Cogan has completed this past year a text on the neurology of the visual system intended to be companion to his previous text on the neurology of the ocular motor system.

Retinal and Choroidal Circulation

Supplementing the morphologic studies on the ocular vasculature, conducted chiefly by Dr. Kuwabara over the past several years, Dr. Friedman has pursued his visualization and measurement of the circulation in vivo. Looking toward a technique that might eventually be applicable clinically, Drs. Friedman, Hugh H. Kobald, and Taylor Smith now employ a radioactive inert gas (krypton^{85}) that can be injected into the general circulation. Its "washout" rate from the eye can then be measured by a Geiger-Müller probe placed over the sclera. The result is a curve having several components which can be resolved into those reflecting retinal, choroidal, and orbital blood flow. The results indicate that the retina, supplied by both the retinal and choroidal system of vessels, has the highest rate of blood flow of any tissue in the body.

While this technique has the essential merit of obtaining data on the intact eye, ancillary experiments designed to demonstrate and identify the components separately have employed autoradiographs, placement of detectors directly in the choroid and on the retina, and the use of nondiffusible, labelled albumen. Most of these studies have been controlled by correlative measurements on eyes in which the retinal arteries had been occluded by photocoagulation.

Preliminary measurements, believed to be the first quantitative measurements of circulation time within the eye, indicate that the amount of blood flowing through the choriocapillaris in the cat per minute is approximately 10 times the weight of the tissue while that through the retina is approximately 1½ times its weight. Spot

tests on the dog and monkey have indicated similar ratios but considerably different ratios for the rabbit. Another set of comparisons in the cat which these studies have permitted is that three times as much blood passes through the choriocapillaris as passes through the retina.

Optics and Instrumentation

The desirability of having a means for taking photographs with the slit-lamp is self-evident. Heretofore, the insufficiency of light in a slit beam and unavoidable movements of the eye to be pictured have combined to thwart the development of any practical means. Using a strobe light for focussing as well as for photography, Dr. Donaldson has adapted to slit-lamp photography a technique he had previously found successful for fundus photography. He now is able to obtain good pictures regularly with his experimental camera model making it possible for the first time to collect a series of slit-lamp photographs. This set will be comparable to those which he has collected for anterior segments and ocular fundi.

The teaching value of these stereophotographs is inestimable. The number of clinical "cases" in these files representing anterior segment disease amounts to approximately seven thousand while those of fundus disease amounts now to more than two thousand. Many have been selected for a special teaching collection and, with the assistance this past year of Dr. Roberts, have been further supplied with case histories and clinical discussions. A few photographs are being published in a new monthly series called "Feature Photo" in the Archives of Ophthalmology. These, too, may constitute a permanent collection for an eventual atlas.

Immunology and the Cornea

Immunologically determined reactions in the cornea probably underlie many of the failures in corneal grafting and in many types of keratitis. In an attempt to suppress the so-called rejection reaction, Drs. Liebowitz and Elliott have found that intramuscular injection of the antimetabolite, 6-mercaptopurine, will prevent an experimentally induced hypersensitivity of the cornea and that none of the animals so treated has developed circulating antibodies. Present studies aim toward determining the effect of time of treatment on the clinical course.

An incidental byproduct of these studies was the discovery that a typical antigen-antibody ring in the rabbit cornea (the Wessely phenomenon) could be produced by a heterograft. This is the first demonstration of soluble antigen diffusing from grafted corneal tissue into the recipient of the graft.

To determine the site of the immunologically responsive cells, Drs. Elliott and Liebowitz are currently irradiating the eyes of some animals and of the whole animal exclusive of the eyes in other animals. It is hoped to ascertain thereby whether the cells producing antibody arise in the cornea as widely believed or in the rest of the body as some of the present investigators' evidence would suggest.

Photoreceptive Abiotrophy in the Dog and Retinitis Pigmentosa

For the past several years Drs. Cogan and Kuwabara have been interested in a naturally occurring retinopathy in the dog as a paradigm for retinitis pigmentosa in human beings. The disease is genetically determined and makes its first appearance at 6–8 months of age with night blindness, narrowing of retinal arteries, and extinction of the electroretinograms. Since it affects the outer layers of the retina preferentially, we have chosen to call it photoreceptive abiotrophy.

Breeding difficulties held up the project for a while but we have now been able to study the eyes of five dogs representing various stages of the disease. The eyes have been subjected to histologic, histochemical and electron microscopic study. First results suggest that no morphologic abnormality may be detected by light microscopy at a stage when the animals first show signs of night blindness and when ophthalmoscopy reveals initial narrowing of the arteries. On the other hand, electron microscopy in these early stages reveals fragmentation and disorganization of the outer segments of the rods and cones with secondary pleating of the inner surface of the pigment epithelial cells. Later stages show loss of photoreceptors and gliosis of the entire retina. These early observations will, of course, have to be tested on further eyes before final acceptance.

Miscellaneous

Several investigations, not intimately related to the foregoing major topics, can be mentioned only in passing if this Report is to be

kept within reasonable bounds. Many of these are studies initiated by trainees and usually prompted by a specific clinical problem. These studies include: Dr. Garcia's investigations of ocular tolerance to metallic foreign bodies, the relationship of intraocular pressure to systemic steroids, and the ocular abnormalities in a single large kindred with von Hippel-Lindau's disease; Drs. Aaberg and Petersen's evaluation of oral glycerine as an agent to deepen the anterior chamber; Dr. Lessell's radiautographic determination of the localization and persistence of topically administered norepinephrine and his histochemical study of the extraocular muscles in various myopathies and neuropathies; Drs. Hutchinson and Frederick's double-blind study of the treatment of hyphemas; and Drs. Howard, Hutchinson, and Frederick's study of changes in the angle of the anterior chamber resulting from blunt injuries and the relationship of these changes to glaucoma. Some of these studies will yield positive results, some will not; and all are being carried out in conjunction with pressing clinical activities that are estimated to require something in excess of 70 hours per week!

TEACHING AND TRAINING

Although the teaching of students is primarily a responsibility of the Department of Ophthalmology, the Howe Laboratory is an active and interested participant.

Undergraduate teaching at the Harvard Medical School has undergone major changes this past year and Dr. Alfred Scott has represented ophthalmology in the reorganization. Instead of the six one-hour lectures previously given to the third year class, ophthalmology now has five three-hour sessions for didactic and laboratory instruction. These are given to the entire class and emphasize the techniques and hazards of the ophthalmic examination. Some time during the subsequent year of clinical clerkship the students have ten half days at the Infirmary for practical exercises (in groups of 4–5 students) and for seminars (in groups of 9–10 students). While the logistics are necessarily complex and, even with the best of execution, can give the student only a superficial comprehension of ophthalmology, we are hopeful that the new system will preserve the favorable features of the previous curriculum and perhaps add some strength in closer student-faculty relationships. The elec-

tive period in the fourth year was not changed this past year but we have submitted proposals for a more comprehensive course that would include instruction of the basic sciences in ophthalmology in addition to the primarily clinical orientation.

The perennial space problem for post-graduate teaching improved considerably this past year when, through Dr. Henry Allen's initiative, new quarters were released in the basement of the Nurses' Residence. The remodelling of this space was made possible by donations obtained by Dr. Allen and established as the Ophthalmic Teaching Fund.

Under the present system of the Infirmary's residency training, about one half of the residents spend one and sometimes two years in the Howe Laboratory under NIH sponsorship prior to their clinical apprenticeship. This acquaints the trainees with research methodology and critique. It frequently launches them on a plan of research which can be carried on subsequently in conjunction with their hospital functions and consolidates what may be a lifelong interest in clinical or laboratory research. The frequent reference in this Report to work that was initiated by these pre-residency trainees speaks for the effectiveness of this system.

In addition to these trainees several Fellows are attached to the Laboratory for one or more years after they have finished their clinical training. During the past year Drs. Mount, Goldstein, and Bland have been Fellows with a special interest in neuro-ophthalmology while Drs. Peczon and Jocson have been Fellows with special interest in glaucoma.

To increase the pool of potential technicians and scientists many institutions offer on-the-job training for college and pre-college students during their summer vacation months. We have done this for a few individuals in the past, some of whom have either returned to us or gone on to related positions elsewhere. This past year four students received experience in histopathology under the tutorship of Dr. Kuwabara while two students joined forces with the Biochemistry Section.

Teaching aids have long been a preoccupation of some members of the Howe Laboratory. The stereoscopic slides of Dr. Donaldson are in daily use. The large collection in the Laboratory is documented with pertinent data and discussions. These slides are used by visiting ophthalmologists, Fellows, post-graduate students, and

senior medical students. Some duplicates are also deposited in the Howe Library for use of junior medical students.

Adding to the three atlases which have been previously prepared (neuro-ophthalmology, gonioscopy, and corneal dystrophies), Dr. Donaldson has now prepared a fourth illustrating the ocular manifestations of systemic disease. Like the others, this consists of 40 stereoscopic slides, a descriptive text, and a viewer — sold at cost by the Massachusetts Eye and Ear Infirmary.

One of the now widely advocated solutions for early detection of glaucoma in the general public is to train all physicians to do tonometry. Toward this end Dr. Scott has incorporated tension taking in his laboratory sections for undergraduate medical students and Dr. Donaldson put on a do-it-yourself exhibit in conjunction with the annual three day meeting of the Massachusetts Medical Society in 1964.

What is believed to be the first formal application of programmed instruction in ophthalmology got under way this past year under the tutelage of Drs. Reinecke and Robert Herm. By programmed instruction is meant the use of machines for that part of didacticism which involves the simple transmission and correlation of facts. We do not wish to take a stand yet whether it is good or bad pedagogy but we do feel it is worth a trial and it is receiving wide attention in other academic circles. Accordingly a series of instructional plates on refraction were prepared and tried out in the post-graduate course. Half of the class used them while the other half served as controls. The results were thought sufficiently good to warrant a text. This will be published in 1965 under the authorship of Drs. Reinecke and Herm. A similar venture on programmed teaching of strabismus is also to be tried out by Drs. Reinecke and David Miller.

Over the past nine years ophthalmic biochemistry conferences have been held in the Boston area under the chairmanship of Dr. Kinoshita. These were begun when ophthalmic biochemists were few and had little contact with each other. The conferences served a useful purpose in promoting the stature of this subspecialty and in integrating the investigators in this field. Such conferences are now thought to be unnecessary and to have grown to such a size

that they no longer serve the original purposes. The conference this past year was therefore the last of these Boston meetings. Like the proverbial dinosaurs they had grown too large to adapt themselves most effectively to the changing needs. But also like the dinosaurs they merit some place in our historical chronicles.

ORGANIZATION AND SERVICE ACTIVITIES

Although basic research has properly been held to be the Laboratory's primary responsibility, clinical studies have been prominent in its activities, as these Reports will attest. This has been possible through the close operation of the Laboratory and clinical services at the Infirmary with many of the staff holding joint appointments. We are not sure that it is wise to have a common Chief for both but that is the way it is for the present.

As a result of our efforts to obtain eyes for corneal transplants, research, and pathologic study, approximately 10% of all autopsies now include examination of ocular tissue. This is a considerable improvement over the past but short of the need and less than in some other enlightened parts of the country. Attempts are currently being made to increase the percentage through education of the public and of physicians.

A long felt need was partially met this past year by establishing a department of illustration and photography. Under the supervision of Mr. Jerome Glickman this is a valuable adjunct to the Laboratory but under the terms of its funding by the General Research Support Grant its services must be limited to research oriented activities.

Those interested in clinical research at the Infirmary have long been handicapped by not having an adequate diagnostic index for out-patients. It means little to have 50,000 visits per year unless an index of these patients and their diseases is recorded in a suitable file. Now, thanks to the initiative of Drs. Reinecke and John Carroll, an ophthalmic indexing system has been established which will permit retrieval of records for any disease category.

The Howe Library is a busy center of bibliographic activity. In the past year it has served more than 8,000 reader-visits, circulated more than 4,000 items, and added 280 new volumes to its shelves.

Under Mr. Charles Snyder's effective guidance the Library took on the additional task this year of the Infirmary's Archives – collecting, cataloging, and storing documents and memorabilia relative to the Infirmary. Less officially but none the less certainly Mr. Snyder has contributed heavily to the historical legacy of ophthalmology as a national consultant and as the author of a monthly series of articles in the Archives of Ophthalmology.

APPOINTMENTS, SPECIAL LECTURES, AND AWARDS

Dr. Friedman was one of four Americans selected by the American Microcirculatory Society to be sent to the International Congress on Microcirculation in Jerusalem last March. There he presented a paper on choroidal microcirculation in vivo. Dr. Kupfer was Visiting Professor in the Department of Anatomy, University College, London for two months during which time he presented a series of lectures on the anatomy, physiology, and biochemistry of the visual system. Dr. Kuwabara was an invited participant at the second International Symposium of Histo- and Cytochemistry in Frankfurt, Germany, and Drs. Futterman and Kuwabara were invited participants at the International Symposium on Biochemistry of the Retina in London. Dr. Cogan was a Visiting Faculty Member at the Mayo Clinic in September and in October he delivered the Montgomery Lecture of the Royal College of Surgeons in Ireland. He was also elected to honorary membership in the Swedish Medical Society. Mr. Charles Snyder was an invited delegate to the XIX International Congress for the History of Medicine, held in Basel, Switzerland. Dr. Grant is ophthalmic consultant to the United States Pharmacopeia and to the Council on Drugs of the American Medical Association. Drs. Grant and Donaldson, along with Dr. Paul A. Chandler, were presented with testimonial gifts by the New England Ophthalmological Society for their contributions to the teaching programs of the Society. Dr. Kinoshita was elected to the Board of Trustees of the Association for Research in Ophthalmology. All of which means the Howe Laboratory is not a hermitage.

FINANCES AND SUPPORT

Without the generous and continued support of individual benefactors, foundations, and government, we would be able to accomplish little. Research on the eye is a combined effort of many each of whom adds what he or she has for the common good. Organizations generally support the long-term projects that comprise the bulk of solid research, individual benefactors generally provide the uncommitted funds for pioneer explorations, the Medical School and Infirmary provide the suitable environment, and the staff, technicians, and ancillary personnel provide the talents and industry which make this great effort productive and worthwhile. The staff joins me in acknowledging with gratitude the many who have so generously supported the Howe Laboratory this past year:

For General Expenses

Individual benefactors

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Research to Prevent Blindness, Inc.

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The Frederick E. Weber Charities Corporation

For Specific Projects

The Fight for Sight
- A study of retinitis pigmentosa in dogs

National Science Foundation
- Development of equipment for producing stereograms

William H. Reisner Foundation
- Equipment of photographic laboratory

Research to Prevent Blindness, Inc.
- Ninth Conference on Biochemistry

Alfred P. Sloan Foundation
- Basic experimental studies in glaucoma

U. S. Atomic Energy Commission
- The carbohydrate metabolism of ocular tissue

U. S. Public Health Service
- General Research Support Grant
- Ophthalmology Training Grants
- Electron microscopy of retinal dehydrogenases
- Metabolic histochemistry of the retina
- Pressure regulating mechanisms in glaucoma
- Research Career Development Award

Experimental cataracts
Lens protein and glutathione
Lipid synthesis of non-adipose tissue
Instrumentation in the field of ophthalmology
Photographic recording of ophthalmic disease
Control of intraocular pressure
Projection of the human retina on the lateral geniculate nucleus
Retinal metabolism
Retinal microcirculation
Ocular blood flow
Corneal lipids

And, finally, it is a pleasure to acknowledge the invaluable assistance of the following secretaries, technicians, students, and ancillary personnel whose efforts contributed much to the successful operation of the Howe Laboratory this past year: Margaret M. Acheson-Donato, Sarah R. Adams, Patricia J. Aitken, Virginia C. Ayres, Elisabeth L. Barrows, Inez M. Berry, Barbara D. Bridgman, Irene V. Brown, Paul L. Bumpus, Priscilla Cogan, Mary Jo Dangerfield, Marie Davenport, Helen A. Day, Claude Delise, Elias Dikmak, Kathryn Donaldson, Joseph A. Gagliardi, Jr., Jerome Glickman, Ellen Goldsmith, Jean Grant, Jeffrey M. Grant, Phyllis Henri, John F. Jope, Hisako Kawakami, Roy G. Kidwell, John E. Kimura, Mary Klein, Irod Lindsey, Thomas P. Lloyd, Jr., Mona E. MacDonald, Alexander J. MacPherson, Anna Marchurs, Allyn Marty, Carol McCune, Patricia R. McSweeney, Alva S. Mendels, Gloria J. Merola, Sharon Mills, Charles Mokeler, Werner Mueller, Jr., Setsuko S. Oak, Patricia Palmer, John M. Parson, E. Joann Perkins, Wanda Pilarski, Walter Pollock, Peter Poulimenos, Mary L. Pruyn, James M. Rabb, Marjorie E. Saunders, Deanna Shapiro, Malcolm W. Swan, Bill Tung, Cynthia Vanden Burg, Olga Wehm-Dalton, Pauline Welsh, Suzanne M. Westerberg, Mary E. Wheeler, Deborah Willard, Pao-Hsi Yeh, Billie-Louise G. Young.

David G. Cogan, M.D.
Director

PUBLICATIONS

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Horse serum and horse sense. 71:155, February 1964.
Conferences on diabetes. 71:295–296, March 1964.
Scientific exhibits. 71:453–454, April 1964.
The tissue committee. 71:610, May 1964.
Heterozygosity. 72:1–3, July 1964.
Woods-Friedenwald Memorial. 72:153, August 1964.
Commemorating the AOS Centenary. 72:295–296, September 1964.
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Grant, W. M.

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Distribution of beta-glucuronidase activity in rat tissues employing the naphthol AS–BI glucuronide hexazonium pararosanilin method. J. Histochem. Cytochem. 12:659–669, September 1964.

Kinoshita, J. H.

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with Merola, L. O.: Hydration of the lens during various stages of galactose cataract. Invest. Ophthal. 3:577–584, December 1964.

Knox, D. L.

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Kroll, A. J.

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Kupfer, C.

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Lessell, S.

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LECTURES

ANDREWS, J. S.

with Futterman, S.: Vitamin A esterification in the retina. Ophthalmic Biochemistry Conference, in Dedham, Massachusetts, February 22, 1964.

with Futterman, S.: Vitamin A esterification in the retina. Federation of American Society for Experimental Biology, in Chicago, Illinois, April 17, 1964.

Corneal lipids. Postgraduate Course in Ophthalmology, Harvard Medical School, September 8, 1964.

COGAN, D. G.

Neuro-ophthalmology Course, University of Miami, in Miami, Florida, January 6–10, 1964:
The retina.
Brain stem and cerebellum.

Putting N.I.H. grants into effect at the laboratory level.
National Advisory Neurological Diseases and Blindness Council, in Bethesda, Maryland, March 20, 1964.

Lectures to the Third Year Class, Harvard Medical School:
Neuro-ophthalmology. April 30, 1964.
The eye and degenerative diseases. May 1, 1964.

with Donaldson, D. D., Kuwabara, T. and Marshall, D.: Keratinizing cystic dystrophy of the corneal epithelium. American Ophthalmological Society, in Hot Springs, Virginia, May 28–30, 1964.

Ocular motor short circuits. Mayo Clinic, in Rochester, Minnesota, September 21, 1964.

The Montgomery Lecture, 1964: Ophthalmic manifestations of bilateral, non-occipital cerebral lesions. Irish Ophthalmological Society, in Dublin, Ireland, October 8, 1964.

Participant, American Medical Association Forum, in Chicago, Illinois, November 1, 1964.

Observations on retinal vasculature. Harvard Medical Society, November 10, 1964.

DONALDSON, D. D.

Monthly Clinical Conferences, New England Ophthalmological Society, October 1963–April 1964.

Postgraduate Course in Ophthalmology, Harvard Medical School:
Corneal dystrophies. January 17 and December 9, 1964.
Systemic disease. January 22 and December 17, 1964.
Anterior chamber angle. February 5, 1964.
Iris tumors. February 10, 1964.
Anterior chamber and iris. November 20, 1964.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
Disc and macular lesions. January 16, 1964.
Iris tumors. February 13, 1964.
Lesions of the chamber angle. March 19, 1964.
The eye and systemic disease. July 7, 1964.

Collagen diseases of the eye. Arthritis Unit, Massachusetts General Hospital, January 27, 1964.

Mexico and points South. New England Ophthalmological Society, March 18, 1964.

Determination of corneal thickness. Ophthalmic Plastics Laboratory, Massachusetts Eye and Ear Infirmary, March 20, 1964.

Lesions of the disc and macula. Presbyterian Hospital, in New York, New York, March 30, 1964.

Wilmer Institute, in Baltimore, Maryland, April 10–11, 1964:
Ocular signs of systemic disease.
Corneal dystrophies and degenerations.
Pathology of the optic disc.

Lesions of the chamber angle and iris. Manhattan Eye and Ear Infirmary, in New York, New York, April 15, 1964.

External and anterior segment manifestations of systemic diseases. University of Missouri, in Columbia, Missouri, April 23, 1964.

Some unusual ocular conditions. St. Louis Ophthalmological Society, in St. Louis, Missouri, April 23, 1964.

Corneal dystrophies and degenerations. New York Alumni Day, New York Eye and Ear Infirmary, in New York, New York, April 27, 1964.

Effects of radiant energy on the eye. Industrial Hygiene Course, Harvard Medical School, May 15, 1964.

External diseases of the eye. Series of lectures to the Lancaster Courses in Ophthalmology, in Waterville, Maine, July 13–16, 1964.

Ocular photography. Postgraduate Course, University of Pennsylvania, in Philadelphia, Pennsylvania, September 28, 1964.

Techniques and diagnoses on gonioscopy. American Academy of Ophthalmology and Otolaryngology, in Chicago, Illinois, October 19–22, 1964.

ELLIOTT, J. H.

Adjuvant uveitis in rats. Ocular Microbiology and Immunology Group, in Miami Beach, Florida, April 20–21, 1964.

Experimental uveitis. House Officer Lecture, Massachusetts Eye and Ear Infirmary, June 16, 1964.

Uveitis, with special emphasis on pathology. Postgraduate Course in Ophthalmology, Harvard Medical School, November 21, 1964.

FRICKER, S. J.

Cortically evoked potentials from visual stimulation. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 27, 1964.

FRIEDMAN, E.

Ocular blood flow. House Officer Lecture, Massachusetts Eye and Ear Infirmary, January 9, 1964.

Choroidal vascular patterns in hypertension. New England Ophthalmological Society, February 19, 1964.

The ophthalmologist's role in the rehabilitation of the blind patient. Peripatology Students, Massachusetts Eye and Ear Infirmary, March 5, 1964.

Choroidal microcirculation *in vivo*. Third European Microcirculatory Conference, in Jerusalem, Israel, March 17, 1964.

with Kopald, H. H. and Smith, T. R.: Ocular circulation *in vivo*. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 27, 1964.

with Kopald, H. H. and Smith, T. R.: Retinal and choroidal blood flow determined with Krypton^{85} in anesthetized animals. Association for Research in Ophthalmology, in San Francisco, California, June 22, 1964.

with Smith, T. R.: Senile changes of the choriocapillaries of the posterior pole. American Academy of Ophthalmology and Otolaryngology, in Chicago, Illinois, October 21, 1964.

Clinical and pathological findings in hypertension. Medical Grand Rounds, Massachusetts General Hospital, December 3, 1964.

Choroidal vascular patterns. New England Ophthalmological Society, December 16, 1964.

Lectures to the Third Year Class, Harvard Medical School:
Diseases of retina and choroid. December 12, 1964.
Ocular motility. December 19, 1964.

with Smith, T. R.: Pathology. Postgraduate Course in Ophthalmology, Harvard Medical School, November–December 1964.

FUTTERMAN, S.

with Andrews, J. S.: The fatty acid composition of human retinal vitamin A ester and the lipids of human retinal tissue. Association for Research in Ophthalmology, in San Francisco, California, June 22, 1964.

Morphology and biochemistry of the retina. Postgraduate Course in Ophthalmology, Harvard Medical School, September 14–15, 1964.

Stiochiometry of retinal vitamin A metabolism during light adaptation. Symposium on the Biochemistry of the Retina, in London, England, September 23, 1964.

GRANT, W. M.

Postgraduate Course in Ophthalmology, Harvard Medical School:
Congenital glaucoma. February 12, 1964.
Toxicology. October 20 and 21, 1964.
Glaucoma. December 16, 1964.

Department of Pharmacology, Harvard Medical School, Second Year Class:

Pharmacology of the eye. February 18, 1964.
Laboratories. October 27 and November 3, 1964.

with Chandler, P. A.: Glaucoma Course. New England Ophthalmological Society, April 25 and 26, 1964.

Current status of glaucoma research. N.I.H. Conference on Glaucoma, in Santa Barbara, California, June 25, 1964.

Practical aspects of tonography and tonometry. House Officer Lecture, Massachusetts Eye and Ear Infirmary, July 16, 1964.

Toxicology, tonometry and tonography. Series of lectures to the Lancaster Courses in Ophthalmology, in Waterville, Maine, August 20–21, 1964.

HAYASHI, M.

The cytologic demonstration of N-acetyl-beta-glucosaminidase employing naphthol AS-BI N-acetyl-beta-glucosaminide and hexazonium pararosanilin. Fifteenth Annual Meeting of the Histochemical Society, in Chicago, Illinois, April 12, 1964.

Histochemical localization of beta-glucuronidase. International Congress of Histochemistry and Cytochemistry in Frankfurt, Germany, August 20, 1964.

KINOSHITA, J. H.

Metabolism of the retina. Postgraduate Course in Ophthalmology, University of California, Los Angeles, in Westwood, California, April 8, 1964.

Galactose cataract. Department of Ophthalmology, University of Chicago, in Chicago, Illinois, April 15, 1964.

Chairman, Ninth Conference on Ophthalmic Biochemistry, in Dedham, Massachusetts, February 21–23, 1964.

Alpha-aminoisobutyric acid uptake by the lens. Federation of American Society for Experimental Biology, in Chicago, Illinois, April 16, 1964.

Osmotic changes in galactose cataract. Association for Research in Ophthalmology, in San Francisco, California, June 22, 1964.

Postgraduate Course in Ophthalmology, Harvard Medical School:
Physiological chemistry of the cornea. September 3, 1964.
Lens and cataracts. September 17, 1964.

Pathways of glucose metabolism. Lens Symposium, in Minneapolis, Minnesota, December 4, 1964.

KUPFER, C.

Studies on the lateral geniculate nucleus. Neuropathology Seminar, Massachusetts General Hospital, January 9, 1964.

Ophthalmology, Third Year Class, Harvard Medical School, February–March, 1964.

The lateral geniculate nucleus: Histological and cytochemical changes following afferent denervation and visual deprivation. Association for Research in Ophthalmology, in New York, New York, April 10, 1964.

Anatomy, physiology and biochemistry of the visual system. Series of lectures, Anatomy Department, University College, in London, England, June–July 1964.

Postgraduate Course in Ophthalmology, Harvard Medical School:
Physiology of aqueous humor. October 8–9, 1964.
Electrophysiology. November 6, 1964.

Kuwabara, T.

Vascular pathology. Postgraduate Course in Ophthalmology, Harvard Medical School, January 2, 1964.

Histochemistry of the retina. Neurology and Children's Service Research Conference, Massachusetts General Hospital, April 16, 1964.

with Carroll, J. M.: Classification of the limbal epithelioma. Histological study. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 27, 1964.

Corneal wound healing, epithelial sliding. Corneal Symposium, in Sudbury, Massachusetts, May 15, 1964.

Aberrant lipogenesis of the cornea, electron microscopic study. Association for Research in Ophthalmology, in San Francisco, California, June 21, 1964.

Armed Forces Institute of Pathology, in Washington, D.C., July 13–18, 1964:

Choroidal vasculature.
Retinal vessels, normal and developmental.
Retinal vessels, pathological conditions.
Retinal histochemistry.
Corneal wound healing.

Histochemistry of the retinal capillary. Second International Congress of Histochemistry and Cytochemistry, in Frankfurt/Main, Germany, August 17, 1964.

Diabetic angiopathy. Conference at the Second Medinische Klinik, University of Frankfurt, in Frankfurt, Germany, September 10, 1964.

Some aspects of retinal metabolism revealed by histochemistry, Müller cells in the pathological condition. First International Symposium on the Biochemistry of the Retina, in London, England, September 24, 1964.

Diabetic retinopathy. Seventh Pan-American Congress of Ophthalmology, in Montreal, Canada, October 15, 1964.

Pathology of diabetic retinopathy. Pathology Conference, New England Deaconess Hospital, December 11, 1964.

Leibowitz, H. M.

The suppression of corneal hypersensitivity with 6-mercaptopurine. Ocular Immunology-Microbiology Meeting, in Miami Beach, Florida, April 20, 1964.

Antimetabolite suppression of corneal hypersensitivity. Corneal Research Meeting, in Sudbury, Massachusetts, May 16, 1964.

Hypersensitivity in the Cornea. House Officer Lecture, Massachusetts Eye and Ear Infirmary, June 9, 1964.

Lessell, S.

with Kuwabara, T.: Phosphatase histochemistry of ocular tissue. Association for Research in Ophthalmology, in New York, New York, April 9, 1964.

Reinecke, R. D.

Refraction. Postgraduate Course in Ophthalmology, Harvard Medical School, February 1964.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
Malingering. March 5, 1964.
Squint symposium — a report. May 12, 1964.
Prevention of complications in corneal lacerations. July 1964.

with Beyer, C.: Treatment of the lacerated cornea. New England Ophthalmological Society, December 16, 1964.

Robb, R. M.

with Kuwabara, T.: Corneal wound healing: A study of the cellular components using tritiated thymidine. Association for Research in Ophthalmology, in New York, New York, April 9, 1964.

Snyder, C.

Sangui-suction — A vanishing art. New England Ophthalmological Society, January 15, 1964.

Trachoma and the immigration laws of the United States. Nineteenth International Congress for the History of Medicine, in Basel, Switzerland, September 11, 1964.

The literature of otolaryngology. Residents in Otolaryngology, Massachusetts Eye and Ear Infirmary, October 24, 1964.

Spector, A.

The incorporation of labeled amino acids into lens protein. Association for Research in Ophthalmology, in San Francisco, California, June 22, 1964.

The effect of actinomycin D and puromycin upon RNA and protein metabolism. Ophthalmic Biochemistry Conference, in Woods Hole, Massachusetts, August 1–2, 1964.

Postgraduate Course in Ophthalmology, Harvard Medical School:
Corneal collagen. September 8, 1964.
Lens proteins. September 22, 1964.

The soluble proteins of the lens. Lens Symposium, in Minneapolis, Minnesota, December 4, 1964.

Thoft, R. A.

The effect of calcium on the permeability of the lens to carbohydrates. Ninth Conference on Ophthalmic Biochemistry, in Dedham, Massachusetts, February 1964.

with Kinoshita, J. H.: Effect of calcium on permeability of rat lens. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 27, 1964.

The rate of potassium exchange of the lens. First International Conference on Ophthalmic Biochemistry, in Woods Hole, Massachusetts, August 1–2, 1964.

The effect of calcium on rat lens permeability. Association for Research in Ophthalmology, in Minneapolis, Minnesota, November 30, 1964.

FORM OF BEQUEST

The Howe Laboratory of Ophthalmology is an independent department of the Harvard Medical School and is jointly supported by a restricted endowment of Harvard University and by the Massachusetts Eye and Ear Infirmary.

For the information of those who may wish to contribute to this Laboratory, a form of bequest is here set forth:

I Give and Bequeath to the Howe Laboratory of Ophthalmology ..... Dollars to be Applied to the Uses of Said Laboratory.

Such bequests are managed by the Treasurer's Office of Harvard University, and the income is accredited to the Laboratory.